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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of CEDGARD

Application No.: 09/465,667 Art Unit: 1651
Filed: December 17, 1999 Examiner: Afremova
Title: METHOD FOR THE PRODUCTION OF TABLETS BY PRESSING
AND TABLETS PRODUCED BY THE METHOD

BRIEF ON APPEAL

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This is appellant's brief, filed in triplicate, to the Board of Patent Appeals and Interferences in support of the patentability of the claims in the above-identified application. This appeal stems from the Office Action mailed September 16, 2004, finally rejecting claims 11, 12, 14-21, 29 and 30 of the subject application. A Notice of Appeal from the final rejection was timely filed with the United States Patent and Trademark Office via facsimile on December 10, 2004. Please charge the requisite small entity fee set forth in 37 C.F.R. §1.17(c) as well as any additional fees required for or incurred as a result of this communication to Deposit Account No. 501249, referencing our docket number 74706.

REAL PARTY IN INTEREST

All rights to the subject application were assigned, via an unrecorded assignment, from the named inventor to Wasa Medicals AB, a company incorporated in Sweden. Wasa Medicals AB is the real party in interest to the above-identified patent application.

RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences related to this application known to appellant, appellant's legal representative, or appellant's assignee and no decision in any other appeal or interference impacts the decision in the present appeal.

STATUS OF CLAIMS

The application contains claims 11, 12, 14-27 and 29-32. Claims 22-27, 31 and 32 are allowed. Claims 11, 12, 14-21, 29 and 30 stand finally rejected under 35 U.S.C. §103(a) as unpatentable over US 4,396,631 taken with US 5,536,526, US 5,531,989, US 5,422,346, US 4,021,545 and US 4,806,368. Appeal is taken from the final rejection of claims 11-12, 14-21, 29 and 30, which claims are set forth in the attached Appendix.

STATUS OF AMENDMENTS FILED SUBSEQUENT TO FINAL REJECTION

There were no amendments presented subsequent to the final rejection mailed September 16, 2004.

SUMMARY OF THE INVENTION

The present invention is directed to a method of producing tablets which include live bacteria. The method comprises mixing at least one strain of live bacteria with at least one fructose oligosaccharide and compressing the mixture to form a tablet having a friability of 0.1-1.0 while maintaining at least about 60% viability of the bacteria following the compression. According to certain embodiments of the invention, the live bacteria may be lactic acid producing bacteria and/or the fructose oligosaccharide may be inulin.

At page 4, lines 8-12 of the instant application, one advantage of the invention is summarized as follows: "The tablets according to the present invention have a lower hardness due to the lower punching pressure when the tablets are formed but an increased viability for the strain of bacteria, which makes every tablet more efficient than conventional tablets." Further, on page 5, lines 24-28, a benefit of the present invention is described thus: "the new method results in an increased maintained viability after tablet punching of up to 200% compared with

conventional tablet fillers. The increased yield results in an appreciably better economy and quality improvement of the above products.”

ISSUES

Whether claims 11, 12, 14-21, 29 and 30 are patentable under 35 U.S.C. §103(a) over the combination of US 4,396,631 taken with US 5,536,526, US 5,531,989, US 5,422,346, US 4,021,545 and US 4,806,368, and more particularly whether the combination of US 4,396,631, US 5,536,526, US 5,531,989, US 5,422,346, US 4,021,545 and US 4,806,368 renders the aforementioned features of the present invention obvious.

GROUPING OF THE CLAIMS

Appellant concede, for the purposes of this appeal, that the claims stand or fall together as grouped.

ARGUMENT

The rejection of claims 11, 12, 14-21, 29 and 30 under 35 U.S.C. §103(a) as being anticipated by US 4,396,631 taken with US 5,536,526, US 5,531,989, US 5,422,346, US 4,021,545 and US 4,806,368 is improper because the references are not properly combinable and further because even assuming, *arguendo*, the analogous references were combined, they fail to disclose each and every element of the invention as claimed.

Deficiencies in the Individual References

US 4,396,631

The reference discloses mixing live bacteria with polysaccharides and providing the mixture, optionally, as a tablet, with the goal of long-term viability of the bacteria. This goal is achieved through the use of select pre-dried substances in addition to the bacteria and the basic compounding material.

US 4,396,631 fails to positively set forth limitations or recommendations for the friability of tablets produced with the described mixture. The absence of any disclosure related to friability can be a result of the fact that tabletting is optional and not a critical step of the methods disclosed therein (see, *inter alia*, column 3, lines 28-32).

US 4,396,631 does not teach or even suggest the use of fructose oligosaccharide or inulin in the method for making hard tablets with live bacteria. Instead, it is the specific, disclosed pre-dried substances which, when present in particular amounts, provide the long-term viability that is the goal of the reference. For example, Example 1 uses 0.2 parts bacteria, 90.3 parts basic compounding material, 7 parts corn starch with 0.5% water content and 2.5 parts other (Column 4, lines 54-58).

Further, US 4,396,631 does not teach or even suggest a tablet with at least about 60% viability of bacteria following compression. There is a disclosure of 2×10^8 bacteria after tabletting (column 4, line 62). This measurement is used to compare the viability over time, as the number given for comparison is that of live bacteria after three months of storage, likely due to the fact that the reference is directed to solutions for long-term viability, not viability in the tabletting process. Without a disclosure of the number of bacteria per gram prior to tabletting, it is impossible to know if the reference teaches a method which, while still failing to disclose elements of the invention as noted above, does touch on the at least about 60% viability limitation presently claimed.

Thus, US 4,396,631 fails to teach or suggest friability limitations, fructose oligosaccharides or inulin in the mixture, and high viability after tabletting, all of which form elements of the present invention.

US 5,536,526

The reference is directed to granulate compositions which can be used for direct compression tablets where sugar alternatives, particularly alternatives which do not induce dental caries, are preferred. US 5,536,526 does not teach or even suggest live bacteria in the tablets. Therefore, it further fails to teach or even suggest at least about 60% viability of bacteria following compression.

US 5,536,526 discloses friability in the range of 0-3 (column 4, line 7). However, there is no discussion of whether this friability range would be appropriate for tablets which have live bacteria and long-term viability, as is the goal of US 4,396,631.

US 5,422,346

The reference is directed to methods of pressing juice to form inulin tablets. US 5,422,346 does not teach or even suggest compressed tablets with a friability between 0.1 and 1.0. Hardness is discussed; however, as noted in US 5,536,526, hardness and friability are two separate considerations (see US 5,536,526, column 3, lines 52-53). Friability is not discussed in US 5,422,346.

US 5,422,346 does not teach or even suggest compressed tablets with live bacteria, therefore the reference also fails to teach bacterial viability of about at least 60% following compression. US 5,422,346 discusses bacteria, however, it is in the context of detailing the relevance of maintaining healthy intestinal bacterial flora, one method of which is to consume the inulin tablets disclosed therein. There is no suggestion that inulin tablets would be useful in a compressed tablet with live bacteria.

US 5,531,989

The reference discloses dietary supplements comprising dietary fiber and immunoglobulin, live bacteria are optionally provided.

US 5,531,989 does not teach or even suggest forming tablets. Thus, the reference further fails to teach or even suggest compressed tablets with a friability between 0.1 and 1.0. The US 5,531,989 composition, instead, is provided as a liquid or as a powder intended to be reconstituted for administration in liquid form.

US 5,531,989 does disclose compositions containing bacteria, however, because the reference fails to teach or even suggest tabletting it furthermore fails to teach that at least about 60% of the live bacteria are viable after tabletting.

US 4,021,545

The reference discloses compounds which can be used to inhibit the mammalian complement system. The compounds may be mixed with inulin and formed into tablets.

US 4,021,545 fails to teach or even suggest compressed tablets with a friability between 0.1 and 1.0. Hard shell capsules are discussed; however, it is not clear from the disclosure whether the intention is a hard shell capsule filled with the composition or whether it is a capsule-shaped form with a hard shell. Regardless, as

noted in US 5,536,526, hardness and friability are two separate considerations (see US 5,536,526, column 3, lines 52-53). Friability is not discussed in US 5,422,346.

US 4,021,545 fails to teach or even suggest compressed tablets with live bacteria, therefore the reference also fails to teach bacterial viability of about at least 60% following compression.

US 4,806,368

The reference is directed to dietary fiber tablets which contain live bacteria. US 4,806,368 does not teach or even suggest the use of fructose oligosaccharide or inulin in the method for making hard tablets with live bacteria.

Further, US 4,806,368 does not teach or even suggest compressed tablets with a friability between 0.1 and 1.0.

Impropriety of the Combination of References

The references cannot properly be taken as a whole. The references which might be combinable, taken together, do not teach or even suggest the claimed invention. In the final rejection, US 4,396,631 is relied upon as a primary reference, and is combined with a series of unrelated references in a hindsight attempt to re-create the invention at the time of filing. This rejection is improper and should be withdrawn.

US 4,396,631 is directed to live-bacteria containing mixtures, optionally tablets, which have good long-term viability. It does not positively set forth limitations or recommendations for the friability of tablets produced with the described mixture. It does not teach or even suggest the use of fructose oligosaccharide or inulin in the method for making hard tablets with live bacteria. It does not teach or even suggest a tablet with at least about 60% viability of bacteria following compression.

US 4,806,368 also discloses tablets with bacteria but not inulin. In that regard, it might be combined with US 4,396,631 by a skilled worker, however, it does not remedy the significant deficiencies in the US 4,396,631 disclosure.

US 5,536,526 discloses tabletting techniques related to friability. The compositions disclosed therein include neither inulin nor live bacteria. It is not proper to combine US 5,536,526 with US 4,806,368 as the former is not related to the unique technical problem of live bacteria in tabletted form. Nothing in the US

5,536,526 disclosure would lead a skilled worker to expect that the methods taught therein would allow for the formulation of a live bacteria-comprising tablet with long-term viability. Thus, the combination of references is improper.

US 5,422,346 and US 4,021,545 are directed to inulin-containing tablets which do not contain live bacteria. A skilled worker attempting to formulate an improved composition for long-term viability of live bacteria-comprising compositions (as taught in US 4,396,631) would not look to the disclosures of US 5,422,346 and US 4,021,545. As with US 5,536,526, there is nothing in the disclosure of either 5,422,346 or US 4,021,545 that would lead a skilled worker to expect that the compositions or methods taught therein would allow for the formulation of a live bacteria-comprising tablet with long-term viability.

Further, US 5,422,346 teaches away from combination with US 4,396,631 by teaching, as pointed out in the Office Action at page 3, fourth full paragraph, that the inulin tablets described therein do not require additional binding materials, such as starch (column 8, lines 41-44). It is the starch component of 4,396,631 that is essential for the long-term viability of the bacteria in the tablets, removal of which would defeat the purpose of the composition disclosed therein. Thus, there is no motivation in US 5,422,346 to modify US 4,396,631 in an attempt to render part of the claimed subject matter obvious.

US 5,531,989 discloses a composition of live bacteria and inulin, which composition is not tabletted. If a skilled worker were following the non-tabletted teachings of 4,396,631, they might possibly look to US 5,531,989 for guidance, however, for the purposes of rendering the present invention obvious US 5,531,989 is a completely irrelevant, non-analogous reference and should not be considered.

It is not only Appellant's view that the references are not properly combinable and, those which might be combined, do not suggest the claimed subject matter. Attention is drawn to the Declaration of Henning G. Kristensen under 37 C.F.R §1.132 ("Kristensen Declaration"), filed April 7, 2004 in the instant case. Dr. Kristensen is a skilled worker in the relevant art as described in paragraph numbers 2-4 of the Kristensen Declaration.

In paragraph number 5, Dr. Kristensen declares: "a person having ordinary skill in the art of pharmaceutical formulation would not have combined the features of the cited patent references to arrive at the invention" and supports the statement with further remarks in paragraph 21: "there would not be any motivation or

guidance apparent to a person of average skill in the art to combine the six references. Adachi [US 4,396,631] and Reddy [US 4,806,368] disclose tablets with bacteria but not inulin. Mitchell [US 5,422,346] and Nair [US 4,021,545] disclose tablets with inulin but not bacteria. Paul [US 5,531,989] discloses bacteria and inulin but not in a tablet, and Virtanen [US 5,536,526] discloses tablets but without inulin or bacteria.”

Dr. Kristensen goes on to declare in paragraph 22: “[b]ased on the references available at the time of the invention, it was not known that the claimed method of producing tablets including live bacteria and supporting substance, *e.g.* inulin, where the tablet has a friability of 0.1-1.0 and maintains at least about 60% viability of the bacteria following the tablet formation was possible. But the claimed method can be performed and results in a product with unexpected benefits, including high bacterial viability. From my knowledge and experience, I know that bacterial survival in conventional tablets is approximately 20%, so the about 60% viability of the claimed method is unexpected and remarkable.”

SUMMARY

The appellant has established that the rejection of claims 11, 12, 14-21, 29 and 30 in the final action mailed September 16, 2004 is improper. In sum, the references are not properly combinable and, even if combined, they fail to teach each and every limitation of the claims as they currently stand.

In view of the foregoing, Appellant requests an order directing withdrawal of the standing rejection and issuance of a notice of allowability.

Respectfully submitted,

February 14, 2005



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In re Patent Application of CEDGARD

Application No.: 09/465,667

Art Unit: 1651

Filed: December 17, 1999

Examiner: Afremova

Title: METHOD FOR THE PRODUCTION OF TABLETS BY PRESSING
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APPENDIX TO BRIEF ON APPEAL

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P.O. Box 1450
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Sir:

The claims on appeal are as follows:

11. A method of producing a tablet including live bacteria comprising the steps:
 - a) mixing at least one strain of said live bacteria with at least one fructose oligosaccharide to form a mixture,
 - b) compressing said mixture so as to form said tablet having a friability of between 0.1 and 1.0 while maintaining at least about 60% viability of said bacteria following the compression.
12. The method of claim 11 wherein said fructose oligosaccharide is present in an amount of about 40 – 99.5% by weight of said tablet.
14. The method of claim 11 wherein said fructose oligosaccharide is inulin.
15. The method of claim 11 wherein said bacteria are lactic acid producing bacteria.

16. A method of producing a tablet including live bacteria comprising the steps:
 - a) mixing at least one strain of live lactic acid producing bacteria with at least one fructose oligosaccharide to form a mixture; and
 - b) compressing said mixture so as to form said tablet having a friability of between 0.1 – 1.0 while maintaining at least about 60% viability of said lactic acid-producing bacteria.
17. The method of claim 16 wherein said fructose oligosaccharide is inulin.
18. The method of claim 16 further comprising adding at least one pharmaceutically acceptable additive to said bacteria and said fructose oligosaccharide prior to said pressing step.
19. The method of claim 16 further comprising adding microcrystalline cellulose to said bacteria and said fructose oligosaccharides prior to said pressing step.
20. The method of claim 16 further comprising adding starch to said bacteria and said fructose oligosaccharide prior to said pressing step.
21. The method of claim 16 further comprising adding calcium diphosphate to said bacteria and said fructose oligosaccharide prior to said pressing step.
29. The method of claim 11, wherein the friability of the tablet is between 0.3 and 0.5.
30. The method of claim 16, wherein the friability of the tablet is between 0.3 and 0.5.